Amendment To The Claims

Listing of the Claims

1. (Currently amended) A mouse, comprising at least one cell that comprises a human chromosome fragment that is not integrated into the mouse cell genome, wherein the human chromosome fragment expresses at least one human cytochrome CYP3A4 family ~~P450 3A family~~ gene.

2. (Canceled)

3. (Previously Presented) The mouse of claim 1, wherein said human chromosome fragment is introduced by microcell fusion using the chromosome fragment.

4. (Previously Presented) The mouse of claim 3, wherein the mouse is a chimeric mouse.

5. (Currently Amended) A mouse, which is obtained by mating a wild-type mouse of the same kind as the mouse of claim 4 with the mouse of claim 4 and which harbors a human chromosome fragment containing a human cytochrome CYP3A4 family ~~P450 3A family~~ gene that is not integrated into the mouse cell genome.

6. (Withdrawn) A nonhuman mammalian according to claim 1, wherein a cytochrome P450 gene inherent to said nonhuman mammalian that is a homolog of said human cytochrome P450 gene has been disrupted and expression of the inherent gene has been reduced or lost.

7. (Canceled)

8. (Canceled)

9. (Currently Amended) A cell~~, organ,~~ or tissue obtained from the liver or small intestine of the mouse of claim 1, wherein the cell or tissue ~~and which~~ is capable of expressing the human cytochrome CYP3A4 family ~~P450 3A family~~ gene.

10. (Withdrawn) A method for preparing a physical map for determining arrangement of mouse Cyp3a genes on a chromosome, comprising the steps of: (a) screening a mouse BAC library by PCR or hybridization using PCR primers or a probe for hybridization for specifically detecting each mouse Cyp3a genes; (b) repeating a cycle of screening the BAC library several times to prepare a BAC contig, the cycle comprising determining a terminal nucleotide sequence of the BAC clones selected in the above step and preparing a primer or a probe based on the nucleotide sequence; and (c) determining both ends of a Cyp3a gene cluster by preparing a full-length cDNA probe of an unprescribed mouse Cyp3a gene and performing hybridization of the above-mentioned BAC contig using the probe under the gentle conditions.

11. (Withdrawn) A physical map which can be prepared by the method according to claim 10 and having elucidated the arrangement of the mouse Cyp3a genes on the chromosome.

12. (Withdrawn) A method of preparing a targeting vector for deleting mouse Cyp3a genes, comprising cloning a genome DNA corresponding to respective terminals of a mouse Cyp3a gene cluster based on the physical map according to claim 11 and inserting each of the obtained cloned fragments into a vector containing a loxP sequence, which is a recognition sequence of recombinase Cre derived from bacteriophage P1.

13. (Withdrawn) A pair of targeting vectors for deleting mouse Cyp3a genes that can be prepared by the method according to claim 12, wherein the respective vectors are to be incorporated in a mouse chromosome and only when said enzyme Cre is present, homologous recombination occurs between the loxP sequences, thereby deleting the whole Cyp3a gene cluster.

14. (Withdrawn) A method of deleting Cyp3a genes of a mouse cell, comprising the steps of introducing the vector according to claim 13 into a cell retaining pluripotency of a mouse and expressing enzyme Cre.

15. (Withdrawn) A mouse cell that can be prepared by the method according to claim 14, being deficient in Cyp3a genes and retaining pluripotency.

16. (Withdrawn) A method of preparing a knockout mouse deficient in Cyp3a genes, comprising the step of differentiating the mouse cell according to claim 15.

17. (Withdrawn) A chimeric mouse or a progeny thereof prepared by the method according to claim 16, being deficient in Cyp3a genes.

18. (Withdrawn) A mouse or a progeny thereof deficient in Cyp3a genes, obtained by mating the chimeric mouse according to claim 17 or a progeny thereof with a wild-type mouse.

19. (Withdrawn) A tissue derived from the chimeric mouse according to claim 16 or a progeny thereof or the chimeric mouse according to claim 17 or a progeny thereof.

20. (Withdrawn) A cell derived from the chimeric mouse according to claim 16 or a progeny thereof or the chimeric mouse according to claim 17 or a progeny thereof.

21. (Withdrawn) A mouse or a progeny thereof obtained by mating the mouse according to claim 8 or a progeny thereof with the chimeric mouse according to claim 17 or a progeny thereof, or the mouse according to claim 18 or a progeny thereof, the mouse or a progeny harboring a human chromosome containing human P450 genes and being deficient in mouse Cyp3a genes.

22. (Withdrawn) A method of producing biologically active human cytochrome P450, comprising the steps of cultivating an individual, tissue or cell of the mouse according to claim 8 or a progeny thereof, expressing the human cytochrome P450 genes harbored therein to produce biologically active human cytochrome P450, and recovering the human cytochrome P450.

23. (Withdrawn) A method of producing biologically active human cytochrome P450, comprising the steps of cultivating an individual, tissue or cell of the mouse according to claim 21 or a progeny thereof, expressing the human cytochrome P450 genes harbored therein to produce biologically active human cytochrome P450, and recovering the human cytochrome P450.

24. (Withdrawn) A method of examining pharmacological effect and/or metabolism of a drug, comprising the step of administering the drug to an individual, tissue or cell of the mouse according to claim 8 or a progeny thereof or the mouse according to claim 21 or a progeny thereof.

25. (Currently Amended) The mouse according to claim 1, wherein the expression of the human cytochrome CYP3A4 family ~~P450 3A family~~ gene is regulated by the expression control region of the human cytochrome CYP3A4 ~~P450 3A~~ gene and is induced by a compound which induces the expression of a human cytochrome CYP3A4 family ~~P450 3A family~~ gene.